REMARKS

Claim of Priority under 35 U.S.C. §120

Applicants have amended the specification to include a claim of priority to co-pending U.S. Application No.10/806,523 filed on March 23, 2004, with a title of "MIXTURES OF CALCITONIN DRUG-OLIGOMER CONJUGATES COMPRISING POLYALKYLENE GLYCOL, USES THEREOF, AND METHODS OF MAKING SAME" now U.S. Patent No. 7,084,121, which in turn is a continuation of application No 09/873,777 filed on June 4, 2001, now US Patent No. 6,713,452. Applicants are entitled to claim priority to this application because there is at least one common inventor and the specification provides ample support for the composition and methods of the presently claimed invention. Notably, the Office pointed to this support by requiring applicants to file a Terminal Disclaimer disclaiming any patent term extending beyond the expiration date of U.S. Patent No. 7,084,121 which is a continuation application of U.S. Patent No. 6,713,452 and thus both specifications are exactly the same with an effective filing date of June 4, 2001. Clearly, the prior application 10/806,523 having a priority date of June 4, 2001 provides ample support for the compositions and methods as described and recited in the presently claimed application.

Thus, the present application is entitled to the effective filing date of June 4, 2001 because U.S. Patent No. 7,084,121 has a priority date of June 4, 2001. Applicants have included herewith a petition under 37 CFR 1.78((a)(3) to the Commissioner for Patents, requesting the acceptance of an unintentionally delayed claim under 35 USC 120 (Appendix A). Further, applicants have included a statement that the entire delay between the 371 filing date of December 22, 2005 of the present application and the date of filing this petition of July 6, 2009 was unintentional. As such, applicants respectfully request that all claims recited in the present application be given the effective filing date of June 4, 2001.

Objection of Claims

According to the Office, applicants must change the use of the terms "amine function of Lys^{11}" to amine group of Lys^{11}." The use of the term "function" was included in issued patent 6,713,452, which is the priority application for issued patent No. 7.084,121, and thus, for this current application due to the above-discussed delayed priority claim, as shown below in issued claim 1:

What is claimed is:

1. A substantially monodispersed mixture of conjugates, wherein the conjugate comprises a first oligomer and a second oligomer, wherein each oligomer comprises a polyethylene glycol moiety and is coupled to salmon calcitonin and wherein the first oligomer is covalently coupled to an amine function of Lys^{11} of the salmon calcitonin and the second oligomer is covalently coupled to an amine function of Lys^{18} of the salmon calcitonin.

Applicants are well aware that patentability of a claim is not controlled by the fact that similar claims have been allowed in the Patent Office, since each claim must be patentable in its own right. However, as stated by the Court in *In re Bisley*, 954 USPQ 80, 83 (CCPA 1952) similar claims allowed by the Patent Office Tribunals furnish evidence of what features those tribunals regarded as patentable, and the court determined it was proper and in fact sometimes necessary to consider allowed claims in order to fully determine what the examiner has determined to be patentable and to maintain continuity in prosecution. Thus, this objection should be withdrawn.

Rejection of Claims and Traversal Thereof

In the March 4, 2009 Office Action,

Claims 1 and 3 were rejected under 35, U.S.C.§112, second paragraph;

Claim 1, was rejected under 35 U.S.C.§102(e) as being anticipated by Soltero et al, (US Patent No. 6,770,625);

Claim 1was rejected under 35 U.S.C.§102(a)or (e)/103(a) as being anticipated or made obvious by Lee et al (US Patent No. 6,506,730):

Claim 1 was rejected under 35 U.S.C.§103(a) as being obvious over Russo (US Patent No. 5,976,788) in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003));

Claim 2 was rejected under 35 U.S.C.§103(a) as being obvious over Russo (US Patent No. 5,976,788) in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003)) and Ekwuribe, et al. (US Patent No. 6,638,906);

Claim 3 was rejected under 35 U.S.C.§103(a) as being obvious over Russo (US Patent No. 5,976,788) in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003)), Ekwuribe, et al. (US Patent No. 6,638,906) and Crotts et al. (US 2003/0017203);

Claims 1-2 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 11 and 12 of US Patent No. 7,084,121; and

Claims 1-3 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38 and 62 of US Patent No. 6,770,625.

Applicants traverse these rejections and insist that none of the cited references defeat the patentability of the presently claimed invention which has an effective priority date of June 4, 2001.

Rejection under 35 U.S.C.§112, second paragraph

Claims 1 and 3 have been amended thereby obviating this rejection. Applicants request the withdrawal of this rejection.

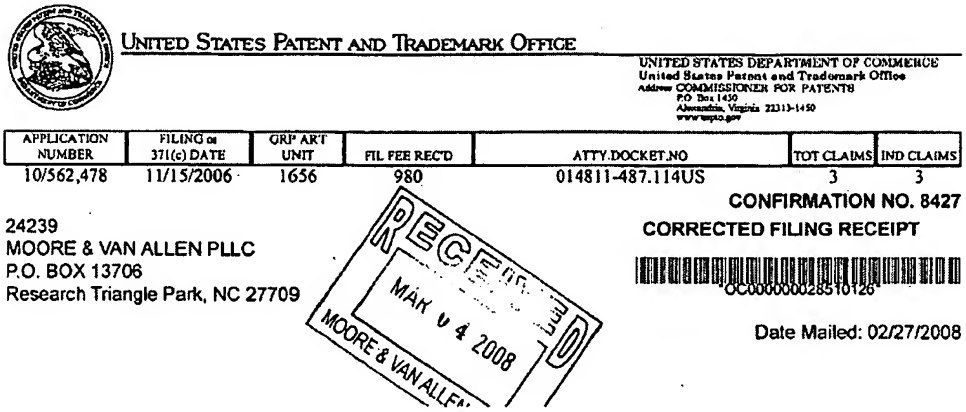
Rejection under 35 U.S.C.§102(e)

Claim 1, was rejected under 35 U.S.C.§102(e) as being anticipated by Soltero et al, US Patent No. 6,770,625 with a filing date of September 5, 2002 and a priority date of September 7, 2001. Applicants submit that this Soltero reference was filed after the effective filing date of the present invention, that being June 4, 2001. This rejection should be withdrawn.

Rejection under 35 U.S.C.§102(e) (a) or 103(a)

Claim 1 was rejected under 35 U.S.C.§102(a) or (e)/103(a) as being anticipated or made obvious by Lee et al (US Patent No. 6,506,730, hereinafter Lee '730). Initially applicants are very concern that the Office really believes that the present application was not filed after November 29, 2000. Clearly

one merely needs to look at the filing receipt for this application where it states the filing date of November 15, 2006 as shown below:



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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
10/562,478	11/15/2006	1656	980	014811-487.114US	3	3

CONFIRMATION NO. 8427

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Applicants insist that Lee '730 does not disclose, teach or suggest the presently claimed invention. Applicants' invention, as set forth in claim 1, describes a method for **orally administrating** to the subject an effective amount of a **substantially monodispersed mixture of conjugates**, wherein the conjugate comprises a first oligomer and a second oligomer. Clearly, the Lee '730 only describes compositions for nasal administration. As such, Lee '730 does not describe each and every element of applicants' claimed invention, and is not anticipatory.

This Lee '730 reference does not teach or suggest the presently claimed invention, but instead teaches away from going in the direction of applicants' claimed invention. Specifically one skilled in the art reading Lee '730 would quickly note that Lee '730 is teaching away from any orally administered compounds. For example, at the bottom of column 1, Lee '730 discusses the disadvantages of oral compounds, as recreated below:

> In fact, the nasal mucosa is a direct absorption route through which drugs can circumvent the liver metabolism, which is a great hindrance to the utilization of drugs in the body upon oral administration. Thus, the nasal transmucosal route has an advantage over the oral route in that the body utilization of drugs can be significantly improved.

Further, Lee '730 reiterates the negative side of oral administration at the bottom of column 3 and recreated below:

> As mentioned above, the nasal transmucosal delivery of peptides alone is significantly improved in absorption efficiency compared with the oral administration because the peptides are not subjected to liver metabolism, but poor in the bioavailability of the peptides because they are degraded by endogenous enzymes.

It is well settled in the law that if a cited reference teaches away from going in the direction of applicants' claimed invention then the Office has not established a *prima facie* case of obviousness. For example, Lee '730 has expressly stated that orally administration of compositions is unacceptable because of the results that occur to the compound in the liver. According to the ruling in *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984), if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. This concept is further addressed in the MPEP, wherein section § 2143.01 V – VI states that:

> "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification."

Thus, the Office has not established a *prima facie* case of obviousness and this rejection must be withdrawn.

Rejections under 35 U.S.C.§103(a)

1. Claim 1 was rejected under 35 U.S.C.§103(a) as being obvious over Russo (US Patent No. 5,976,788, hereinafter Russo '788) in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003)). Applicants insist that this proposed combination does not in any way teach and suggest the presently claimed invention.

Initially, it should be noted that the present invention has an effective filing date of June 4, 2001 and the Komarova reference was not published until June 6, 2003. As such, this Komarova reference is not competent prior art and must be removed from this rejection.

The Office has already admitted that the Russo '788 does not teach use of PEGylated CT for treating pain, wherein the PEGylation includes PEGylation at Lys^{11} and Lys^{18} residues of CT. As the proposed combination does not teach or suggest each and every element of claim 1. Applicants request the withdrawal of this rejection for obviousness.

2. Claim 2 was rejected under 35 U.S.C.§103(a) as being obvious over Russo , 788, in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003)) and Ekwuribe, et al. (US Patent No. 6,638,906, herein after Ekwuribe '906). Applicants insist that the proposed combination suffers from the same shortcomings as that of the obviousness rejection of claim 1.

As previously stated Komarova is not competent prior art and must be removed. Further, Ekwuribe '906 qualifies as a 102(e) reference and under section 103(c) must be disqualified as relevant prior art. Specifically, the present application has an effective filing date of June 4, 2001. The Ekwuribe '906 was filed on December 13, 1999 (before the effective filing date of June 4, 2001 of the present application) but did not publish until October 28, 2003 (after the effective filing date of June 4, 2001 of the present invention). As such the Ekwuribe '906 would be considered to meet the time requirements of a 102(e) reference and was commonly owned by Nobex Corporation, (now both are owned by Biocon Limited) at the effective filing date of the present application. Consistent with the provisions of MPEP §706.02(l)(2), the statement hereinabove by applicants disqualifies U.S. Patent No. 6,638,906 from being used in a rejection under 35 U.S.C. §103(a) against claims of the present application. See also, MPEP §§ 706(l)(1). Accordingly, because the Ekwuribe '906 has been disqualified as a secondary reference, the Office cannot use any teachings in this reference to establish a *prima facie* case of obviousness.

As previously stated, the Office has already admitted that the Russo '788 does not teach use of PEGylated CT for treating pain, wherein the PEGylation includes PEGylation at Lys^{11} and Lys^{18} residues of CT. As the proposed combination does not teach or suggest each and every element of claim 1. Applicants request the withdrawal of this rejection for obviousness.

3. Claim 3 was rejected under 35 U.S.C.§103(a) as being obvious over Russo '788 in view of Komarova et al. (*Calcif. Tissue Int.*73, 265-273 (published on line 6/6/2003)), Ekwuribe '906 and Crotts et al. (US 2003/0017203). Applicants insist that the proposed combination suffers from the same shortcomings as that of the obviousness rejections of claims 1 and 2.

As previously stated Komarova is not competent prior art and must be removed. Further, Ekwuribe '906 has been disqualified under section 103 (c). Notably, the present invention has an effective filing date of June 4, 2001 and the Crotts reference was filed after this effective filing date of the present invention. As such, the Crotts reference is not competent prior art and must be removed from this rejection.

Further, the Office has already admitted that the Russo '788 does not teach use of PEGylated CT for treating pain, wherein the PEGylation includes PEGylation at Lys^{11} and Lys^{18} residues of CT. As the proposed combination does not teach or suggest each and every element of claim 1. Applicants request the withdrawal of this rejection for obviousness.

Obviousness-Type Double Patenting

1. Claims 1-2 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 11 and 12 of US Patent No. 7,084,121. In response, a Terminal Disclaimer is enclosed (Appendix B) and submitted herewith under the provisions of 37 C.F.R. §1.321(c) to overcome the obviousness-type double patenting rejection.

2. Claims 1-3 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38 and 62 of US Patent No. 6,770,625, hereinafter Soltero '625. Applicants vigorously disagree for numerous reasons.

The Office fails to see any patentable differences between the subject matter of the current pending claims of the subject application and the subject matter encompassed by claims 38 and 62 of Soltero '625. Applicants submit that the claims of Soltero '625 differ greatly from the present claims because

all the independent claims of Soltero '625 must include a bile salt as shown below in claim 1 from which claim 38 depends.

1. A pharmaceutical composition comprising:
a drug-oligomer conjugate comprising a drug covalently coupled to an oligomeric moiety and wherein the drug is a calcitonin polypeptide;
a fatty acid component comprising a fatty acid; and
a bile salt component comprising a bile salt; wherein the fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1, wherein the fatty acid component is present in an amount sufficient to lower the precipitation point of the bile salt compared to a precipitation point of the bile salt if the fatty acid component were not present in the pharmaceutical composition, and wherein the bile salt component is present in an amount sufficient to lower the solubility point of the fatty acid compared to a solubility point of the fatty acid if the bile salt were not present in the pharmaceutical composition.

37. The pharmaceutical composition of claim 1, wherein the calcitonin polypeptide is salmon calcitonin.

38. The pharmaceutical composition of claim 37, wherein the drug-oligomer moiety comprises salmon calcitonin coupled to two oligomeric moieties, wherein one oligomeric moiety is coupled to the lysine at the 11 position of the salmon calcitonin, and wherein one oligomeric moiety is coupled to the lysine at the 18 position of the salmon calcitonin.

Further claim 62 teaches the same components, as shown below.

62. A method of treating a bone disorder in a subject in need of such treatment, said method comprising administering to the subject a pharmaceutical composition comprising (a) a therapeutically effective amount of a calcitonin drug-oligomer conjugate that comprises a calcitonin drug covalently coupled to an oligomeric moiety; (b) a fatty acid component comprising a fatty acid; and (c) a bile salt component comprising a bile salt, wherein the fatty acid component and the bile salt component are present in a weight ratio of between 1:5 and 5:1, wherein the fatty acid component is present in an amount sufficient to lower the precipitation point of the bile salt compared to a precipitation point of the bile salt if the fatty acid component were not present in the pharmaceutical composition, and wherein the fatty acid component is present in an amount sufficient to lower the solubility point of the fatty acid compared to a solubility point of the fatty acid if the bile salt were not present in the pharmaceutical composition.

The test for obviousness-type double patenting is whether the claimed invention of the subject application would have been obvious from the subject matter of the claims in the Soltero patent. *See*

In re Longi, 774 F.2d 1100, 225 USPQ 645 (Fed.Cir 1985). Additionally, the Office is not at liberty to resort to the text of the Soltero specification but of course in this situation it does not matter because the specification is completely devoid of any mention of leaving the bile salt out of the conjugate. The Appeal Board recently addressed this very issue in *Ex parte Whalen*, 89 USPQ2d 1078 (Bd. Pat. App. & Int. 2008), and determined that the analyses for obviousness under 35 U.S.C. §103 and obviousness-type double patenting are not identical; for one thing, "[t]he objects of comparison are very different: Obviousness compares claimed subject matter to the prior art; nonstatutory double patenting compares **claims in an earlier patent to claims in a later patent or application**." *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1378 n.1 [68 USPQ2d 1865] (Fed. Cir. 2003) (emphasis added) . The purpose of an obviousness-type double patenting rejection is "to prevent an unjustified extension of the term of the right to exclude granted by a patent by allowing a second patent claiming an obvious variant of the same invention to issue to the same owner later." *In re Berg*, 140 F.3d 1428, 1431 [46 USPQ2d 1226] (Fed. Cir. 1998).

Thus, in all instances, only the literal language of the claims of the US 6,770,625 may be considered in arriving at the conclusion of obviousness-type double patenting. Because the Office has not provided the Applicants with any factual basis and/or rationale to support the conclusion that the presently claimed invention is an obvious variation of the previously issued patent, the double patenting rejection of the present claims cannot stand. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

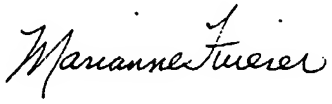
Extension Petition and Fees Payable

Applicants request a one month extension extending the June 4, 2009 deadline to July 4, 2009. Further, applicants have included herewith a Terminal Disclaimer with a fee due of $180.00. Still further, applicants have included herewith a Petition for Delayed Priority Claim with a fee due of $1410.00. All fees are being paid herewith by electronic transfer. If any additional fee is found due for entry of this amendment, the Commissioner is authorized to charge such fee to Deposit Account No. 13-4365 of Moore & Van Allen.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Liu, reconsider the patentability of all pending claims, in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Liu is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,



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